EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	868	514/337.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/10/24 14:59
L2	10757	indazole	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/10/24 14:59
L3	48	l1 and l2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/10/24 15:00
L4	254747	cancer	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/10/24 15:00
L5	29970	l3 an dl4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/10/24 15:00
L6	22	l3 and l4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/10/24 15:00
L7	3180	l2 and l4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/10/24 15:00
L8	162	l2 same l4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/10/24 15:00

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L1              STR
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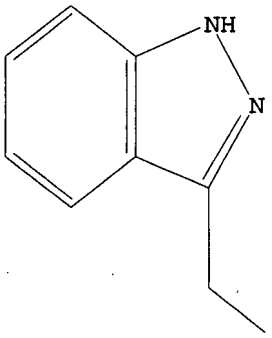

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SAMPLE SCREEN SEARCH COMPLETED -      211 TO ITERATE

100.0% PROCESSED      211 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         3349 TO     5091
PROJECTED ANSWERS:               0 TO        0

L2             0 SEA FAM SAM L1

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SEARCH TIME: 00.00.01

L3             1 SEA FAM FUL L1

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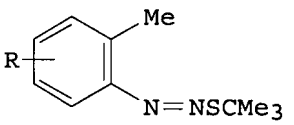
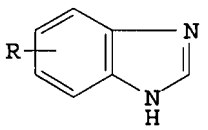
=> s l3
L4 7 L3

=> d ti au abs so py 1-7

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI 7-Nitro indazole derivatives are potent inhibitors of brain, endothelium and inducible isoforms of nitric oxide synthase
AU Bland-Ward, Philip A.; Moore, Philip K.
AB The effect of 7-nitro indazole (7-NI) and a range of substituted indazole derivs. on nitric oxide synthase (NOS) enzyme activity in homogenates of rat cerebellum, bovine endothelial cells and lung from endotoxin-pretreated rats was investigated. 3-Bromo 7-nitro indazole was either equipment (IC50, 0.86 ± 0.05 μM c.f. 0.78 ± 0.2 μM, n = 6, P>0.05) or approx. 4x (IC50, 0.17 ± 0.01 μM c.f 0.71 ± 0.01 μM, n = 6, P>0.05) or 20x (IC50, 0.29 ± 0.01 μM c.f. 5.8 ± 0.4 μM, n = 6, P<0.05) more potent than 7-NI as an inhibitor of bovine endothelial, rat cerebellar and rat lung NOS enzyme activity resp. 2,7-Dinitro indazole also inhibited NOS in all three tissue sources with a potency similar to that of 7-NI. These results suggest that 3-bromo 7-NI and 2,7-dinitro indazole may prove to be useful addnl. tools with which to examine the biol. properties of nitric oxide (NO).
SO Life Sciences (1995), 57(11), PL131-PL135
CODEN: LIFSAK; ISSN: 0024-3205
PY 1995

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI A novel approach to 1H-indazoles via arylazosulfides
AU Dell'Erba, Carlo; Novi, Marino; Petrillo, Giovanni; Tavani, Cinzia
GI

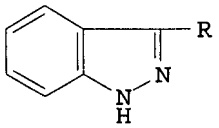


I


II

AB Treatment of variously substituted (o-alkylaryl)azosulfides I (R = H, 3-, 4-, 5-Me, 4-, 5-, 6-Cl, etc.) with potassium tert-butoxide in DMSO at room temperature smoothly furnishes 1H-indazoles II.
SO Tetrahedron (1994), 50(11), 3529-36
CODEN: TETRAB; ISSN: 0040-4020
PY 1994

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI The preparation of certain 3-alkylindazoles
AU Hannig, E.; Kollmorgen, C.; Koerner, M.
GI



I

AB Indazoles I (R = Me, Et, Pr, CHMe2, Bu, CH2CHMe2, CHMeEt) were prepared in 6-52% yield by Grignard reaction of 2-H2NC6H4CN with alkyl halides, diazotization of 2-H2NC6H4COR, and reductive cyclization of 2-RCOC6H4,N2+Cl- with SO2.
SO Pharmazie (1976), 31(8), 534-6
CODEN: PHARAT; ISSN: 0031-7144
PY 1976

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Reactivity of indazoles and benzotriazole towards N-methylation. Analysis of the proton nuclear magnetic resonance spectra of indazoles and benzotriazoles
AU Palmer, Michael H.; Findlay, Robert H.; Kennedy, Sheila M. F.; McIntyre, Peter S.
AB Methylation of 3-, 7-, and 3,7-substituted indazoles in alkaline solution gave mixts. of 1- and 2-Me compds. with the 1-Me isomer predominating except in the 7-monosubstituted cases. INDO calcns. of the electron d. at the N atoms were used to account for the relative reactivities. The PMR spectra of the 1- and 2-methylindazoles differ enough to be used as diagnostic tools for the positions of methylation. A detailed ABCD anal. of some spectra was performed and the results assessed in terms of degree of aromatic character.
SO Journal of the Chemical Society, Perkin Transactions 2: Physical Organic Chemistry (1972-1999) (1975), (15), 1695-700
CODEN: JCPKBH; ISSN: 0300-9580
PY 1975

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Synthesis of tetrahydroindazole derivatives
AU Piozzi, Franco; Umani-Ronchi, Archile; Merlini, Luciana
AB Alicyclic ketone enamines condensed with diazo esters or diazo ketones gave good yields of 4,5,6,7-tetrahydroindazole derivs. The conditions for their dehydrogenation to indazole derivs. were investigated. 1-Pyrrolidinocyclohexene (I) (15.1 g.) in 80 cc. CHCl3 refluxed 2 hrs. with 12.5 g. N2CHCO2Et (II), and the product refluxed 15 min. with 100 cc. H2O and 20 cc. concentrated HCl yielded 10.7 g. 3-carbethoxy-4,5,6,7-tetrahydroindazole (III), m. 89° (hexane). Similar runs with 1-piperidinocyclohexene and 1-morpholinocyclohexene yielded 35 and 2% III, resp. II with the 4-Me derivative (IV) of I, b35 141°, yielded similarly 50% 3-Me derivative (V) of III, m. 114-15° (hexane). AcCHN2 (VI) with II gave 80% 3-acetyl-4,5,6,7-tetrahydroindazole (VII), m. 104° (C6H6). IV with VI yielded 75% 6-Me derivative (VIII) of VII, m. 153°. BzCHN2 (IX) with II gave 70% 3-benzoyl-4,5,6,7-tetrahydroindazole (X), m. 177° (C6H6). IX with IV yielded 60% 6-Me derivative (XI) of VII, m. 190° (C6H6). III (0.97 g.) in 40 cc. CCl4 refluxed 0.5 hr. with 1.8 g. N-bromosuccinimide and 30 mg. Bz2O2, treated with 6 g. AcOK and 4 cc. AcOH, and refluxed 2 hrs., and the product refluxed 8 hrs. with 30 cc. 10% alc. KOH gave about 10% indazole-3-carboxylic acid (XII). III (500 mg.) refluxed 48 hrs. with 200 mg. 10% Pd-C in 6 cc. Decalin yielded 150 mg. microcryst. Et ester of XII, m. 134-5° (EtOH and sublimed at 115°/0.2 mm.), and small amts. 3-methylindazole and III. V yielded similarly 180 mg. 3-carbethoxy-6-methylindazole (XIII), m. 158° (EtOH and sublimed at 120°/0.2 mm.). 5-Me isomer of V gave similarly 80 mg. 5-Me isomer of XIII, m. 151° (EtOH and sublimed at 120°/0.2 mm.). VII (500 mg.) and 200 mg. 10% Pd-C refluxed 48 hrs. in 6 cc. Decalin, and the

crude product chromatographed on Al2O3 yielded 200 mg. 3-ethylindazole (XIV), m. 74-5°, b0.5 100° and small amts. 3-acetylindazole (XV) and unreacted VII. VIII gave similarly during 72 hrs. the 6-Me derivative of XIV, m. 76-7° (petroleum ether), b0.5 110°. X gave during 36 hrs. 150 mg. 3-benzylindazole (XVI), m. 119-20° (hexane), and traces of 3-benzoylindazole (XVII) and unreacted X. XI gave during 36 hrs. 160 mg. 6-Me derivative (XVIII) of XVI, m. 139° (hexane), with traces of unreacted XI. VII (500 mg.), 200 mg. 10% Pd-C, 5 cc. Decalin, and 1.5 cc. Me2C:CHAc refluxed 24 hrs. yielded 200 mg. XV, m. 182° (EtOH). X gave similarly 80 mg. XVII and traces of XV and unreacted X. VIII gave similarly during 60 hrs. 3-acetyl-6-methylindazole, m. 156° (C6H6 and sublimed at 115°/0.2 mm.). XI yielded similarly 3-benzoyl-6-methylindazole, m. 194-5° (C6H6 and sublimed at 120°/0.2 mm.).

SO Gazzetta Chimica Italiana (1965), 95(7), 814-24
CODEN: GCITA9; ISSN: 0016-5603

PY 1965

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

TI Constitution of pyrazoles, indazoles and anthranils

AU v. Auwers, K.

AB cf. preceding abstract Using the data reported in the preceding paper, A. discusses the possible formulas for the pyrazoles, indazoles and anthranils. The original should be consulted for this discussion, as well as for the data on the following compds.: Me2 and Et2 hydrazoisobutyrate, PhNHNH2, PhMeNNH2, PhNHNHMe, PhEtNNH2, PhNHNHEt, o-MeC6H4NHNHPh, PhNMeNHPh, 3-[β- methoxypropyl]-1,2-diphenyl-hydrazimethylene, and the corresponding Et compound, 3-ethylindazole, Et 1-ethyl-indazole-3-carboxylate, Et 2-ethylindazole-3-carboxylate, Et indazole-2-carboxylate, iso-Am indazole-2-carboxylate, anthranil, C-Me and C-Ph derivs., and Et anthroxanate.

SO Ann. (1924), 437, 65-86

PY 1924

L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

TI Structural and spatial isomerism in indazole derivatives and the constitution of indazoles

AU v. Auwurs, Karl; Duesberg, Marianne

GI For diagram(s), see printed CA Issue.

AB cf. C. A. 14, 64. When indazole or its homologs are heated with excess of alkyl iodides at 100° they yield the 2-alkyl derivs. (Schad, Ber. 26, 213(1893)). The 1-alkyl derivs. are obtained much less easily from monoalkyl-o-amino ketones but it has recently been found (cf. C. A. 14, 65, and following abstract) that they are the chief products (66-75%), together with 33-25% of the 2-isomers when the indazoles are alkylated in the presence of alkali. As the 2-alkyl derivs. boil considerably higher than the 1-isomers, the 2 forms can be separated by repeated fractional distillation or by one fractional distillation followed by crystallization or through the picrates, as those of the 2-alkyl compds. at once sep. from Et2O or alc. on addition of picric acid. The constitution of the isomers is established by the fact that the lower boiling forms which are the chief products of alkylation in alkaline solution are identical with the 1-alkyl compds. obtained from alkyl-o-amino ketones; these constitutions were confirmed by degradation of the corresponding CO2H acids; the easily esterified acids, which have the structure I, lose CO2 quant. and yield the lower boiling alkylindazoles, while the difficultly esterified acids of the structure II form the higher boiling isomers with equal ease. There is no such regularity between the m. ps. of the isomeric alkylindazoles as exists between their b. ps., but the picrates of all the 1-alkylindazoles thus far prepared melt lower than their isomers, and are more soluble Alkylation on the N increases the solubility of the indazoles in H2O; this is especially true of the 2-alkyl compds. The mother substances have a sweetish honey-like

odor, the N-alkyl derivs. a quinoline-and alkaloid-like odor.and the Ac derivs. a more or less strong mouse odor. The 2-alkyl compds. are stronger bases than the 1-isomers, dissolving more easily in dilute acids and forming less easily hydrolyzed salts. The formation of the 1-alkyl compds. in alkaline solution is probably due to the intermediate formation of quaternary addition products (III) from the 2-alkyl derivs. first formed. Both the 1-and 2-alkyl indazoles form quaternary salts with alkyl halides, the second alkyl group combining with that N atom to which the first alkyl group is not attached. When, however, both alkyls are the same the resulting quaternary salts are identical, so that one of the 2 systems (III and IV) must rearrange into the other. When these quaternary salts are heated, they lose alkyl halide and form 1-alkylindazoles, indicating that they have the structure III. Picric acid in H2O converts the quaternary iodides quant. into difficultly soluble picrates. 2-Methylindazole can be prepared by heating indazole with 3 parts MeI 6 hrs. at 100° and treating the product in alc. with picric acid (yield of picrate, 90%), by shaking Ag indazole 2 hrs. with 4 mols. MeI, repeatedly extracting with Et2O and fractionating (yield, good), or by heating 2-methylindazole-3-carboxylic acid to 230°; it seps. from low-boiling petr. ether in stout prisms and tables, m. 56°, b. 261°, b16 135°; Schad's product, m. 35°, obtained by crystallization from hot H2O, is a hydrate; the slender leaflets lose approx. 1 H2O in vacuo over H2SO4 and go over into the anhydrous form; with HgCl2 it gives a precipitate of fine needles separating on slow cooling of an aqueous solution in stout prisms, with AgNO3 a precipitate of short prisms; picrate, fine silky yellow needles, m. 168°. 1-Methylindazole, prepared by boiling indazole with 2 mols. MeI and 1.5 atoms Na in absolute MeOH until the solution is neutral, evaporating the alc. and excess of MeI in vacuo, treating with not too much H2O, extracting with Et2O and separating from the 2-isomer by the general methods given above, seps. from petr. ether in porcelain-like flat prisms, m. 60-1°, b. 231°, b17 109°; the HgCl2 compound crysts. in hair-like silky needles from H2O, the AgNO3 compound in fine needles, the picrate in fine yellow needles soon changing into small stout crystals of greater luster, m. 136-7° (the picrate of indazole itself also seps. from Et2O in 2 forms, long slender golden yellow leaflets and fine silky light yellow needles, which, however, are not mutually interconvertible; from alc. it seps. in light yellow lustrous needles at once becoming dull and assuming a golden yellow color on the H2O bath; it m. 136-7°). Heated with 3 parts MeI 6-7 hrs. at 106°, both the 1-and 2-methylindazoles yield 1,2-dimethylindazolium iodide, spears from alc., m. 187°, gradually turns brown in the air and light; picrate, orange felted needles from alc., m. 167-8°. 2-Ethylindazole, faintly colored oil, b. 268°, b14 140°; picrate, fine needles from Et2O, slowly changing into stout crystals, leaflets with golden luster from alc., m. 155-6°. 1-Ethylindazole, b21 126-7°, b727 233-4°; picrate, slender, light yellow, lusterless needles, m. 148-50°. 1-Methyl-2-ethylindazolium iodide, from 1-methylindazole and EtI after 8 hrs. at 100° or 2-ethylindazole and MeI after 4 hrs., delicate needles from alc., m. 172.5-3.0°; picrate, scales with golden luster from H2O, m. 196-7°. 2-Methyl-1-ethylindazolium iodide, m. 154°; picrate, flat orange-yellow needles from H2O, m. 149-50°. 1,2-Diethylindazolium iodide, from the two ethylindazoles and EtI, stout crystals from alc., m. 134°; picrate, fine golden needles from H2O, m. 153°. 2,3-Dimethylindazole, stout crystals from Et2O, m. 79-80°; picrate, fine yellow powder from Et2O or H2O, m. 224-5°. 1,2,3-Trimethylindazolium iodide, delicate silky needles from alc., m. 220-1°. As stated above, these quaternary iodides when heated lose the alkyl on the 2-N atom as alkyl iodide and form the 2-alkylindazole; the 1-methyl-2-ethyl iodide, however, gave about 75% 1-methyl- and 25% 2-ethylindazole. Of the 3 isomeric N-acetylindazoles it had already been shown that the one m. 169-71° is the 1-compound That the isomer m. 42-3° is the 2-compound is indicated by the facts

that it is structurally different from the first, is likewise easily saponified and is formed from indazole in the same way as 2-alkylindazoles. From the ease with which the 3rd isomer, m. 106°, is converted into the stable 2-compound it must be closely related in structure to the latter; as each yields distinct derivs. from which it can be recovered unchanged and as they behave differently towards chemical reagents, they are probably spatial rather than physical isomers. The 2-EtCO and 2-Bz derivs. show the same isomerism phenomena but the ability to form stereomers apparently disappears when the H on the C of the heterocyclic ring is replaced by an alkyl. The stabilities of these labile acyl derivs. vary within wide ranges; it has not yet been established with certainty whether chemical reagents (such as traces of acids or alkalies) catalytically accelerate the rearrangement into the stable forms; I apparently does not. The isomerism is explained by assuming that the valence of the N to which the acyl residue is attached extends in different directions, in the 2 isomers, from the plane of the N. C. N. ring (V and VI). By analogy with the aldoximes the labile acyl derivs. would have the syn- (VI) and the stable isomers the anti-structure (V). When the stable acetate in absolute Et2O is treated a few min. with dry HCl heat is evolved and on cooling the HCl salt seps. in fine needles which become tarry when drained in moist air and on clay soon are completely converted into the original substance. The HgCl2 compound begins to contract 150° and m. 200-10°. The labile is completely converted into the stable compound after 30 min. at 100°; its HgCl2 derivative m. 174-5°; with HCl in Et2O it is saponified to the free indazole-HCl; with AgNO3 in alc. it forms a crystalline compound, m. 128-30°; with H2PtCl4 in concentrated HCl is formed an egg-yellow chloroplatinate, m. 266°, while under the same conditions the stable acetate seps. unchanged as the result of hydrolysis. Stable propionate, from indazole and (EtCO)2O allowed to stand a long time at room temperature or warmed gently and shaken with ice H2O, delicate needles from petr. ether, m. 52°; if the petr. ether solution is allowed to evaporate at room temperature there first sep. long stout prisms which gradually change into small needles; it b. 267°. Labile isomer, prepared like the acetate, pearly leaflets from Et2O or petr. ether on rapid, rhombic or 6-sided tables from Et2O on slow crystallization, m. 100.5-1.5°, b. 267° with complete rearrangement into the stable form. Stable benzoate, from indazole and Bz2O heated 3 hrs. on the H2O bath, extracted with Et2O and freed from BzOH with Na2CO3, fine silky needles from petr. ether, long needles from Et2O, m. 94-5°. Labile isomer, small stout flat crystals from Et2O, m. 78°, dists. as a thick yellowish oil solidifying to crystals of the stable form, but a sample kept 3 months m. about 60°, showing that it still contained some of the labile form, The stable 2-acetyl-3-methylindazole, m. 72-3°, prepared from 3-methylindazole and Ac2O, is also obtained when the indazole is acetylated by the C5H5N method of making the labile isomers; when the 2nd method of preparing labile isomers is used (treatment of the Ag salt with AcCl in Et2O), the chief product is again the stable acetate, although there is formed a small amount of a substance, crystals from Et2O, m. 147° (gas evolution) which, however, does not rearrange into the stable acetate and is therefore not the labile isomer. Similarly, only 1 form of 2-acetyl-3-ethylindazole could be obtained; it seps. from petr. ether in fine prisms or stout crystals, m. 35.5-6.5°, rather difficultly soluble in HCl and repptd. by H2O. In the hope of being able to determine by spectrochem. means to which of the types I and II free indazole and its C-homologs correspond, an indazole of sufficiently low m. p. (3-ethylindazole) was prepared and its spectrochem. consts. were compared with those of a number of 1- and 2-alkylindazoles. The following values of M for α, D, β-α and γ-α, resp., were found for the alkyl derivs.: 1-Et, 44.81, 45.20, 1.51, 2.51; 2-Et, 45.59, 46.03, 1.69, 2.83; 1,3-EtMe, 49.75, 50.16, 1.63, 2.74; 2,3-EtMe, 50.28, 50.76, 1.85, 3.13. Calculating the "theoretical" refractions and dispersions for these substances on the basis of observations on phenylhydrazines and -hydrazones, the average "specific" exaltations for 1-alkylindazoles are

-1.45, -1.55, -27%, -27%, and for 2-alkylindazoles 0.96, 1.00, 18%, 20%, while for 3-ethylindazole they are -0.88, -0.85, -21%, -,and 1.03, 1.14, 9%, -, according as it is assumed that it has the structure of a 1-or 2-alkylindazole. These values agree better if the latter structure is taken as being correct, although the former is not entirely excluded as the derivation of the "theoretical" values for these compds. is as yet uncertain. Another line of evidence, however, tends to confirm the correctness of the above conclusions; if the 3-ethylindazole is imagined as derived from the 1- or 2-isomers by a shifting of the Et from a N to C, then one of the two tert. N atoms becomes sec., and the refraction and dispersion of the 3-compound should differ from those of the isomer from which it is derived by the difference between the refractometric equivs. of these 2 kinds of N atoms. Subtracting the value Ntert. -Nsec., the 1-Et isomer gives 44.48, 44.86, 1.46 and the 2-isomer 45.26, 45.69, 1.64 for Mα, MD, and Mβ -Mα, while the values found for the 3-compound are 45.38, 45.92, 1.56. The chemical evidence also speaks, although not with absolute certainty, in favor of the type II for the structure of indazole. The 3-ethylindazole was prepared by gradually adding 100 g. o-O2NC6H4CO2H to 4 parts SOCl2, occasionally heating in a bath at 80°, removing the excess of SOCl2, by distillation, finally in vacuo in a current of dry air, filtering the dark oily chloride (100 g.), adding 133 g. of this, in 250 cc. Et2O, to a solution prepared from 16 g. Na in 300 cc. Et2O and 100 g. MeCHAcCO2t and converting the resulting dark red oily O2NC6H4COCMeAcCO2Et (yield, 93%) into o-nitropropiophenone by Gevekoht's method (Ann. 221, 323(1883)). The ketone (yield, 40%), a light yellow viscous oil, b15, 166-7°, b10-1 161°, gradually darkens in the air; semicarbazone, needles from alc., m. 182-3°. From 10 g. of the ketone dropped into 74 g. SnCl2 in concentrated HCl and boiled 0.5 hr., with subsequent decomposition with NaOH of the double salt which seps., is obtained 70% of o-aminopropiophenone, slender, faintly yellowish, pearly leaflets with a jasmine odor from dilute alc., m. 46-7°; oxime, fine silky needles from H2O or stout needles from C6H6, m. 88-9°. The NH2 ketone by Fischer and Tafel's method (Ann. 227, 316(1885)) gives 40-50% of crude or 25% of pure 3-ethylindazole, fine needles or stout prisms from ligroin, b. 290°, b15 157-8°, m. 74.5-5.5°; picrate, light yellow needles from alc., m. 152.5-3.5°. 2,3-Diethylindazole, from the 3-ethylindazole with EtI at 100°, b. 287-90°; picrate, flat light yellow needles from H2O, m. 184-6°.

SO Berichte der Deutschen Chemischen Gesellschaft [Abteilung] B: Abhandlungen (1920), 53B, 1179-210
CODEN: BDCBAD; ISSN: 0365-9488

PY 1920

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=> s indazole
          4103 INDAZOLE
          1043 INDAZOLES
L5        4355 INDAZOLE
                 (INDAZOLE OR INDAZOLES)

=> s cancer
        334611 CANCER
         49263 CANCERS
L6      347166 CANCER
                 (CANCER OR CANCERS)

=> s l5 and l6
L7         206 L5 AND L6

=> s l5(n)l6
L8           1 L5(A)L6

=> s l5(p)l6
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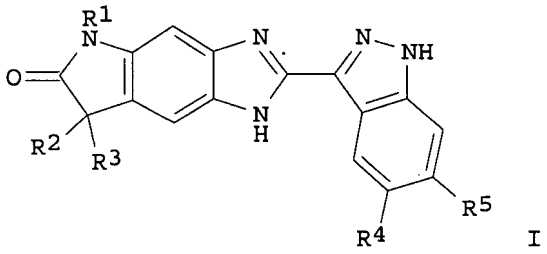
L9 137 L5(P)L6

=> d ti au abs so py 1-5

L9 ANSWER 1 OF 137 CAPLUS COPYRIGHT 2007 ACS on STN
TI Indazoles as Potent and Selective Aurora Kinase Inhibitors
AU Anthony, William
AB Aurora kinases belong to a small family of mitotic serine-threonine kinases. Aurora A, B and C have been implicated in the progression of cancer and over-expression has been seen in several types of solid tumors including breast, ovary, prostate, pancreas and colorectal cancer. As part of our program toward the development of kinase inhibitors as potential anti-cancer therapeutics, we have designed a new series of mols. based on a central indazole scaffold. The synthesis and biol. characterization of these potent Aurora kinase inhibitors will be described as well as the use of structure-based design to modify potency and isoenzyme selectivity.
SO Frontiers in CNS and Oncology Medicinal Chemistry, ACS-EFMC, Siena, Italy, October 7-9 (2007), COMC-044 Publisher: American Chemical Society, Division of Medicinal Chemistry, Washington, D. C.
CODEN: 69KAR2
PY 2007

L9 ANSWER 2 OF 137 CAPLUS COPYRIGHT 2007 ACS on STN
TI Synthesis and Evaluation of Novel 17-Indazole Androstene Derivatives Designed as CYP17 Inhibitors
AU Moreira, Vania M.; Salvador, Jorge A. R.; Njar, Vincent C. O.; Vasaitis, Tadas S.
AB A series of novel 1H- and 2H-indazole derivs. of the com. available dihydroepiandrosterone acetate have been synthesized and tested for inhibition of human cytochrome 17α-hydroxylase-C17,20-lyase (CYP17), androgen receptor (AR) binding affinity and cytotoxic potential against three prostate cancer (PC) cell lines. The synthesized compds. were found not to inhibit C17,20-lyase activity significantly when compared to both ketoconazole and VN/85-1. They also did not display affinity towards the LNCaP mutated AR at the concns. tested. However, the 2H-indazole series was particularly effective against PC-3 cells whereas two compds. of the 1H-indazole series were exclusively cytotoxic towards them. Because PC-3 cells lack the AR, it is likely that mechanisms such as apoptosis or cell cycle arrest account for inhibition of proliferation on this particular cell line.
SO Frontiers in CNS and Oncology Medicinal Chemistry, ACS-EFMC, Siena, Italy, October 7-9 (2007), COMC-011 Publisher: American Chemical Society, Division of Medicinal Chemistry, Washington, D. C.
CODEN: 69KAR2
PY 2007

L9 ANSWER 3 OF 137 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of indazolyl imidazoindolone derivatives for treatment of cancers
IN Georges, Guy; Goller, Bernhard; Limberg, Anja; Rueger, Petra; Rueth, Matthias; Schuell, Christine; Stahl, Mark
GI



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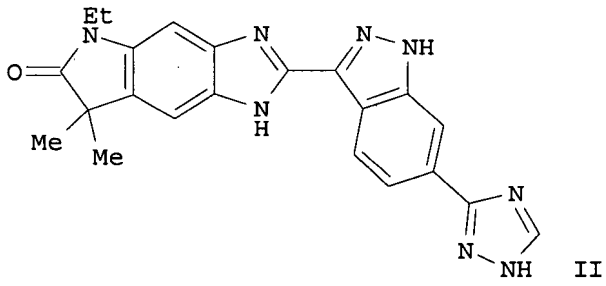


II

AB Title compds. represented by the formula I [wherein R1-R3 = independently alkyl; R4, R5 = independently (un)substituted heteroaryl, Ph, cycloalkyl, etc.; and pharmaceutically acceptable salts thereof] were prepared as Aurora A kinase inhibitors. For example, II was provided in a multi-step synthesis starting from 3,3-dimethyl-6-nitro-1,3-dihydroindol-2-one. II showed inhibition of Aurora A kinase and HCT 116 cell with IC50 values of 0.002 μM and 0.025-1.500 μM, resp. Thus, I and their pharmaceutical compns. are useful as Aurora A kinase inhibitors for the treatment of cancers.

SO PCT Int. Appl., 64pp.
CODEN: PIXXD2

PY 2007

L9 ANSWER 4 OF 137 CAPLUS COPYRIGHT 2007 ACS on STN

TI Inhibitory effect of YC-1 on induction of VEGF and GPI genes in hypoxic human pancreatic cancer cells

AU Du, Jing; Zhao, Qiu; Gu, Hua; Teng, Xiaoli; Qin, Hua; Liu, Nanzhi

AB The objective was to investigate the function and mechanism of 3-(5'-hydroxymethyl-2'-furyl)-1-benzyl indazole (YC-1) on activity of VEGF and GPI genes in human pancreatic cancer PC-3 cells incubated under hypoxic conditions. Human pancreatic cancer PC-3 cells were incubated under hypoxic culture conditions. Immunocytochem. staining was used to detect HIF-1α protein expression in hypoxic and normoxia PC-3 cells. Semi-quant. RT-PCR was used to detect the effect of YC-1 on the expression of VEGF and GPI mRNA HIF-1α protein in PC-3 cells. Effect of YC-1 on the expression of HIF-1α protein was examined by Western blotting. MTT assay was used to detect proliferation of hypoxic PC-3 cells. HIF-1α expression was mainly located in nuclei in hypoxic PC-3 cells. The mRNA synthesis of VEGF and GPI and the protein expression of HIF- 1α were significantly decreased in the group treated with the highest concentration of YC-1 (100 μmol/L). Compared to placebo, YC-1 inhibited the proliferation of hypoxic PC-3 cells greatly when it was increased to 100 μmol/L. YC-1 inhibited the transcription of VEGF and GPI in hypoxic human pancreatic cancer PC-3 cells. It was induced by down-regulation of HIF-1α protein. YC-1 inhibits the proliferation of PC-3 cells exposed to hypoxic conditions.

SO Zhonghua Zhongliu Zazhi (2006), 28(7), 486-489
CODEN: CCLCDY; ISSN: 0253-3766

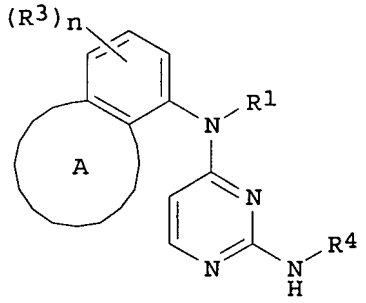
PY 2006

L9 ANSWER 5 OF 137 CAPLUS COPYRIGHT 2007 ACS on STN

TI Pyrimidine derivatives as EphB4 inhibitors and their preparation, pharmaceutical compositions and use in the treatment of cancer

IN Kettle, Jason Grant; Read, Jon; Leach, Andrew; Barlaam, Bernard Christophe; Ducray, Richard; Lambert-Van Der Brempt, Christine Marie Paul

GI



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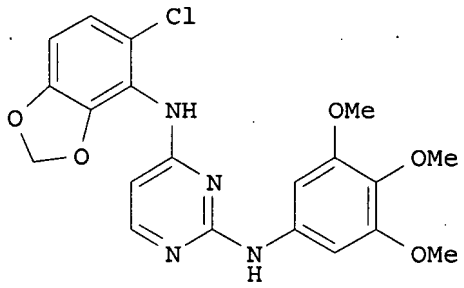

II

AB The invention concerns benzamide compds. of formula I, or a pharmaceutically acceptable salt thereof.,. The invention also relates to processes for the preparation of such compds., pharmaceutical compns. containing them and their use in the manufacture of a medicament for use as an antiproliferative agent in the prevention or treatment of tumors or other proliferative conditions which are sensitive to the inhibition of EphB4, and/or EphA2 and/or Src kinases. Compds. of formula I wherein R1 is H, (un)substituted C1-6 alkyl, (un)substituted C2-6 alkenyl, and (un)substituted C2-6 alkynyl; ring A is (un)saturated (un)substituted fused 5- to 6-membered carbocyclic or heterocyclic ring; each R3 is independently halo, CF3, CN, NO2, etc.; R4 is (un)substituted phenyl; and their pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by amination of 2,4-dichloropyrimidine with (5-chloro-1,3-benzodixazol-4-yl)amine; the resulting 2-chloro-N-(5-chloro-1,3-benzodioxol-4-yl)pyrimidin-4-amine underwent amination with 3,4,5-trimethoxyaniline to give compound II. All the invention compds. were evaluated for their EphB4 inhibitory activity.

SO PCT Int. Appl., 235pp.
CODEN: PIXXD2

PY 2007
2007

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